UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,255	06/28/2007	Sung-Il Roh	K5675.0090/P090	8998

24998 7590 05/21/2009

DICKSTEIN SHAPIRO LLP
1825 EYE STREET NW
Washington, DC 20006-5403

EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
05/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,255	ROH ET AL.	
	Examiner	Art Unit	
	Deborah Crouch	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *20-26 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,27-49 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/06; 10/12/06;7/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election of group I, claims 1-19, 27-49 and 51, in the reply filed on January 8, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 20-26 and 50 are withdrawn from consideration.

For clarity, the claim groups in the restriction/election requirement mailed December 8, 2008 are claims 1-19, 27-49 and 51, Group I; claims 20-24, Group II and claims 25,26 and 50, Group III.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 27-43 and 45-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

At the time of filing the skilled artisan would not have regarded the claimed invention enabled by the present specification. Stojkovic teaches nuclear transfer, where a human ES cells nucleus was transferred into an enucleated human oocyte, resulted in the formation of one blastocyst (page 228, col. 2, parag. 2, lines 9-13). However, the blastocyst degenerated after 48 hours in culture (page 228, col. 2, parag.

2, lines 13-15). The method of Stojkovic does not appear to be reproducible in that only one human blastocyst was formed, and that one died rendering the production of human blastocysts unpredictable. As the claimed method cannot be distinguished from that of Stojkovic, the presently claimed method is unpredictable. In relation to Stojkovic and this enablement rejection, Mitalipov states, concerning attempts to produce Rhesus monkey NT embryos, "NT embryos derived from embryonic, but not from somatic, cells showed the ability to develop to the blastocyst stage in vitro" (page 1371, col. 1, parag. 2, lines 13-18). Mitalipov also states failure to reprogram provides the reason for the lack of blastocyst production (Ibid. and pages 1371-1372, bridging sent.). Thus, Mitalipov states their attempts at producing cloned rhesus monkey blastocysts by SCNT failed; not that the efficiency was low. The teachings of Stojkovic and Mitalipov exemplify the unpredictable nature of primate nuclear transfer. Mitalipov successfully produced cloned rhesus monkey blastocysts using a rhesus monkey embryonic cell (blastomere) as nuclear donor, but Stojkovic could not produce viable clone human blastocysts using a human embryonic stem cell as nuclear donor. Mitalipov clearly states failure in human blastocyst production by SCNT. Thus, at the time of filing, the skilled artisan would have regarded the claimed methods of producing a human blastocyst by SCNT and methods of producing a hES cell line by SCNT unpredictable without undue experimentation.

Others post-filing, however, have shown success at the production of primate blastocyst, and ICM cell cultures from them, albeit by a method not disclosed in the specification. Byrne teaches the successful production of rhesus monkey ES cells from

cloned rhesus monkey blastocyst. The method taught by Byrne uses a method not disclosed in the present specification. Byrne teaches enucleation of rhesus monkey MII oocytes without the use of Hoechst stain to visualize nuclear material (page 500, col. 2, parag. 4, lines 3-5). The Hoechst staining method also requires UV light, which Byrne suggests may additionally damage the primate oocyte (page 500, col. 2, parag. 4, lines 8-11). The enucleation method specifically disclosed in the specification uses Hoechst staining/UV exposure, and indicated to be the most successful (specification, page 11, lines 9-10). Thus, the post-filing art supports the enablement rejection as the method successfully implemented contained a step materially different and separate from that claimed. Further, the specification fails to provide any guidance that the Hoechst was problematic, or methods to over come such a problem.

The claims are drawn to methods of producing hES (human embryonic stem) cell lines by nuclear transfer, where a human somatic cell nucleus is introduced into an enucleated human oocyte, and cultured to the blastocyst stage. At the blastocyst stage, ICM cells are isolated and cultured to form hES cells/cell lines. The specification provides guidance for the claims demonstrating the production, by nuclear transfer, of human cells that exhibit the ability to form teratomas when the cells are injected into the SCID mice. However, the art at the time of filing recognized four criteria for human cells to meet prior to being deemed hES cells. The generic criteria for indicating any cell was an ES cell needed to meet the following:

1. Originate from a pluripotent cell population.
2. Maintain normal karyotype
3. Immortal and can be propagated indefinitely in the embryonic state

4. Clonally derived cultures capable of spontaneous differentiation into extraembryonic tissue and somatic cells representative of all three embryonic germ layers in teratomas or in vitro.

The specification discloses the claimed hES cell line produced from the ICM of NT human blastocysts, and that the cells maintain a normal karyotype. However, the specification does not provide evidence that the hES cell lines are immortal, capable of indefinite propagation or that clonally derived hES cells have the ability to develop into cells representative of all three germ layers. Clonal cells are required to prevent any instance of multipotent cells having been selected. (See Pera, page 6, parag. 2). Thus, it is not clear, in view of Pera, if applicant's hES cells or cell lines meet the criteria for "stem cell" designation.

Further, a post-filing investigation indicates that applicant's hES cells line taught in the specification, deposited under the accession number KCLRF-BP-00092 was not produced by the claimed method. Results indicate the hES cells line is actually the result of parthenogenic activation of a human oocyte (Kitai, page 347, col. 1, parag. 1, Ref. CK, IDS 7/30/08). Further, the investigation discovered that applicant falsified data resulting from the claimed method (Fox, parag. 1 and 5). Therefore, the disclosure cannot be relied upon for providing an enabling method to produce either human blastocysts by nuclear transfer or an enabling method for the production of hES cells/cell lines from NT h-blastocysts. This evidence in addition to the teachings of Stojkovic, Mitalipov, Byrne and Pera, indicate the method claimed for producing human blastocysts by NT and ES cells or cell lines from NT human blastocysts are not enabled.

Thus, because at the time of filing the art taught the unpredictable nature of producing human blastocysts and human ES cells from those blastocysts, the post-filing evidence that applicant's method of nuclear transfer did not result in hES cells, and additional post-filing art demonstrating the production of hES cells from nuclear transfer produced blastocysts using a method not suggested by the present specification, the claimed methods are not enabled. The skilled artisan would have needed to engage in an undue amount of experimentation without a predictable degree of success to implement the invention as claimed. The preponderance of evidence supports the lack of enablement for the breadth of the claims at the time of filing.

A declaration filed under 35 U.S.C. § 1.132 attesting to data demonstrating hES cell production by the claimed method maybe sufficient to overcome the above rejection.

Also, claims 2 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 2 is directed to the hES cell line deposited under the accession number KCLRF-BP-00092. Claim 4 is to a method for preparing an embryonic stem cell line deposited under accession number KCLRF-BP-00092. For enablement, the specification must provide a readily available and reproducible source for the hES cells deposited as KCLRF-BP-00092. The present specification does not provide such a

reproducible source for obtaining the specific hES cell line claimed, and thus KCLRF-BP-00092 must be deposited to meet the requirements of 35 U.S.C. § 112, first paragraph (MPEP 2404.01).

Since evidence is of record that a deposit has been made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the plasmids have been deposited under the Budapest Treaty and that the plasmids will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. 37 CFR 1.808

However, if the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.808, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
(d) a viability statement in accordance with the provisions of 37 CFR 1,807; and
(e) the deposit will be replaced if it should ever become inviable.

As required under 37 CFR 1.809(d), the specification shall contain: (1) the accession number for the deposit; (2) the date of deposit; (3) a description of the deposited biological material sufficient to identify it and to permit its examination; and (4) the name and address of the depository.

The notification of receipt of record is part of the WO document related to this application. Applicant should in response to this rejection, also, file a copy of the receipt as a separate paper.

Thus, the skilled artisan would have needed to engage in an undue amount of experimentation to implement the invention of claims 2 and 4.

The rejections above under 35 U.S.C. § 112, first paragraph may seem contradictory, but compact prosecution requires all reasonable rejections to be made.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 44 and 51 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Thomson et al. Science. 1998, Vol. 282, pages 1145-1147, Ref CB, IDS filed 10/12/06.

Thompson teaches human ES cell lines HI, H7, H9, H13, H14 (page 1145, col. 2, parag. 1, lines 14-17). Whereas the hES cell lines of Thomson were isolated from the ICM of human blastocyst produced by IVF and the claimed hES cells are isolated from

the ICM of human blastocysts produced by nuclear transfer, the specification and the art at the time of filing offer no expectation that the hES cells would be patentably distinct. Any differences would not cause a structural or functional distinction between the hES cell lines of Thomson and those claimed.

Likewise Thomson teaches human blastocysts produced by nuclear transfer (page 1145, col. 2, parag. 1, lines 1-6). Although the human blastocysts taught by Thomson were made by a materially different and separate protocol from the presently claimed blastocyst, which was produced by nuclear transfer, the method of producing the blastocyst is not taught by the specification or the art at the time of filing to affect either the structure or the function of the blastocyst. The blastocysts of Thomson and that claimed are not patentably distinct, with any differences not affecting the structure or function of the blastocysts.

[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

"The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. In re Fessmann, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending

to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983).

"Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972))."

"When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22

USPQ 313 (E.D.N.Y. 1934.) See MPEP 2113 and MPEP 2112.01.

[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

"The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. In re Fessmann, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983).

"Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is

evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

The case law supports the anticipation of the claims by Thomson. Therefore, Thomson anticipates the invention of claims 1, 44 and 51.

Claims 3-19, 43 and 45-49 are free of the prior art. At the time of filing, the prior art did not teach or suggest enabled methods for producing human blastocyst or methods for producing human ES cells or human ES cell lines from NT human blastocysts. The closest prior art is Cibelli et al., Human Somatic Cell Nuclear Transfer, Journal of Regenerative Medicine, 2001, Vol. 2, pp. 25-31, Ref. CI, IDS filed 10/12/06, where it is taught the growth of human NT embryos to the six cell stage (page 29, parag. 1). Blastocysts contain at least 64 cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 6:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/
Primary Examiner, Art Unit 1632

May 21, 2009